OPEN-GLOBE EYE INJURIES AND CHOICE OF MUSCLE RELAXANT: A REVIEW OF THE EVIDENCE

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Abstract

A goal of treatment of open-globe eye injuries is preventing rises in intraocular pressure and the resulting loss of vitreous humor fluid from the eye globe. Surgical repair of these injuries often requires general anesthesia and tracheal intubation. Normal intraocular pressure is 10-22 mm Hg, with variations between daytime and nighttime values. Factors such as eye muscle structure, fluid volume in the eye, overall hemodynamic status, blood acidity, and mechanical pressure collectively contribute to fluid pressure within the eye. One factor that has been shown to be strongly correlated with increased intraocular

pressure is elevated venous pressure with physiological conditions during tracheal intubation (eg, straining, coughing, bucking). To determine intubation best practices, we reviewed the literature on succinylcholine, a depolarizing neuromuscular blocking agent, and nondepolarizing neuromuscular blocking agents. Research and case reports have not shown an association between the loss of ocular contents and succinylcholine administration. However, succinylcholine has been associated with increased intraocular pressure after administration and intubation. Nondepolarizing neuromuscular blocking agents, particularly rocuronium, administered before or instead of succinylcholine, have been found to attenuate the rise in intraocular pressure after induction and intubation.

Keywords
Succinylcholine, nondepolarizing neuromuscular blocking agents, muscle relaxant, tracheal intubation, intraocular pressure, open-globe injury.

Introduction

A goal of treatment of penetrating injuries is avoidance of intraocular pressure (IOP) elevation to prevent loss of vitreous humor fluid from the eye globe.[1] When penetrating open-globe injuries occur, surgical repair often necessitates general anesthesia and tracheal intubation. Normal IOP is maintained at 10-22 mm Hg, with variations in daytime and nighttime values. Multiple factors, including the structure of eye muscles, fluid volume in the eye, overall hemodynamic status, blood acidity, and mechanical pressure, contribute to the amount of fluid pressure within the eye.[2]

One particular factor that has shown a strong correlation with increased IOP is an elevation in venous pressure with physiological conditions that occur during tracheal intubation (eg, straining, coughing, bucking).[2] Patients presenting with ocular trauma involving an open-globe injury require exquisite care and attention from anesthesia personnel to minimize elevations

in IOP above normal ranges and prevent the loss of vitreous humor and, potentially, loss of the contents of the eye. Questions concerning the use of succinylcholine, a depolarizing neuromuscular blocking agent (NMBA), for intubation require a review of the evidence to determine best practice for this patient population. The availability of alternative nondepolarizing NMBAs (eg, rocuronium) for intubation has created an opportunity for improved practice.

History

Succinylcholine is considered the gold standard of NMBAs when the need for rapid sequence intubation (RSI) is present. Succinylcholine allows for quick, optimal intubating conditions when patients present with a need for immediately securing the airway and emergent surgical interventions.[3] Over time, succinylcholine has continued to be associated with an increase in IOP. This association has been through anecdotal professional-to-professional reports and, recently, a single non-confirmatory case study that discusses the loss of vitreous humor after its administration presumably due to brief muscle fasciculations.[3,4,5] Libonati's[6] retrospective study of 250 patients having undergone ocular surgery found that succinylcholine did not cause loss of vitreous humor in any of their patients.

Having been cited 107 times in scholarly literature reflects growing questioning of the belief against succinylcholine's use in this patient population. Alternatively, nondepolarizing NMBAs at above normal doses, allow for comparable intubating conditions to succinylcholine with the theoretical advantage of reducing IOP due to their extraocular muscle relaxing effects with fasiculations.[1] Anesthesia providers are faced with an evidence-based practice conundrum when determining which NMBA to administer for tracheal intubation in this particular patient population. Therefore, this evidence-based review sought to answer the question; in adult patients with open-globe ocular injuries does the administration of succinylcholine for intubation

compared to nondepolarizing NMBAs cause increases in IOP and support the theoretical risk of extrusion of aqueous humor?

Literature Review

An initial, in-depth literature search was conducted without limit to date, utilizing PubMed, Embase, Clinical Key, ProQuest Nursing and Allied Health Source, and Web of Knowledge databases to locate scholarly literature comparing the administration of nondepolarizing NMBAs with succinylcholine in patients undergoing surgical repair for an open-globe injury. The key terms used included "succinylcholine," "suxamethonium," "open-globe injury," "eye injury," "intraocular pressure," "neuromuscular blocking agents," and "aqueous humor." The results from the search did not meet the inclusion criteria, specifically the disclosure of loss of aqueous humor.

Therefore, a second literature search was conducted with a broader approach. A combination of key terms was utilized for each database with the use of AND. The PubMed search was performed with a combination of "open-globe" AND "succinylcholine" AND "intubation" and generated 16 results. Embase was searched with a combination of "succinylcholine," "ocular aqueous humor" AND "IOP," based off of predicted search terms and resulted in 12 scholarly articles for review. A Web of Science topic search was conducted with the combination of "open-globe" and "succinylcholine" that produced 15 articles. The ProQuest database generated predicted search terms, and "eye injur*" AND "succinylcholine" were combined to deliver 9 relevant articles. Clinical Key was searched with the combined key terms "eye injuries and succinylcholine" and refined to anesthesia specialty, and the database produced 29 results. Limiters were applied to each database to include only English-language articles and adult populations (18+ years of age). A cumulative total of 85 articles resulted. After the application of inclusion criteria specific to adult patients undergoing surgical procedures requiring intubation with intraocular pressure monitoring, the

administration of nondepolarizing NMBAs and/or the administration of succinylcholine, a total of 7 articles were found relevant to the purpose of this review. In an attempt to locate additional studies, a Google Scholar search was conducted which produced similar findings.

The case study by Amadasun and Isesele[4] describes a 34-year-old trauma patient admitted to an emergency department with intra-abdominal injuries, limb injuries, and a laceration of the right cornea. The patient required emergency surgical intervention of the abdominal injuries, and the injured eye was dressed with gauze and strapped prior to entering the operating room. Once induction agents were administered, cricoid pressure was applied and 100 mg succinylcholine was administered.

An elevation in blood pressure was noted following intubation, and the patient required additional anesthetic agents post intubation upon the return of spontaneous breathing.[4] Direct visualization of the injured eye was not performed after the dressing application until the completion of the abdominal surgical procedure, and there is no mention of the elapsed time between interventions.[4] After laparotomy, the ophthalmologists reported for the corneal repair, only to find the vitreous humor had been extruded.[4] Mechanical external pressure application to the injured eye such as touching the eye or the structures around the eye, elevation in blood pressure, and tracheal irritation (in this case, external cricoid pressure and intubation) have been shown to significantly elevate IOP, which could have led to the loss of intraocular contents with an open open-globe injury.[2]

A major weakness of this case report is the lack of visual observation of the actual extrusion to identify a cause and effect. Other weaknesses include the application of mechanical pressure, intubation procedures, an abdominal surgical procedure with undisclosed measurement of continual neuromuscular monitoring, and a lengthy period with multiple opportunities for other

contributing factors to the vitreous humor extrusion. Therefore, succinylcholine administration cannot be definitively identified as the cause for the loss of ocular contents in this patient.

Lavery et al[7] conducted a randomized controlled study that compared IOP readings in 30 patients following the administration of atracurium, a nondepolarizing NMBA, or succinylcholine. Ten of the 30 patients were administered induction agents that excluded muscle relaxants followed by laryngoscopy and tracheal intubation. Once a steady state of anesthesia and hemodynamics was achieved, either 0.5 mg/kg of atracurium or 1.0 mg/kg of succinylcholine was administered. IOP readings were obtained at 1-minute intervals for 5 minutes and once more at 10 minutes post intervention. The intervention strategy allowed for the comparison of the two agents under conditions unaffected by extraneous factors such as tracheal irritation or hemodynamic instability. The findings of the steady state groups indicated that succinylcholine administration was responsible for a significant ($P<0.025$) elevation in IOP regardless of tracheal manipulation. The remaining 20 patients were administered either a combination of atracurium 0.75 mg/kg and thiopentone 5 mg/kg or succinylcholine 1.0 mg/kg and thiopentone 5 mg/kg prior to tracheal intubation, which was performed with cricoid pressure application.

IOP readings were then obtained over 1-minute intervals for 5 minutes post intubation. Thiopentone produced a significant ($P<0.025$) decrease in IOP post induction; however both groups displayed a significant ($P<0.005$) elevation in IOP immediately following tracheal intubation. In the atracurium group, IOP readings did not breech baseline values. Immediately following intubation, the succinylcholine group displayed a significant ($P<0.05$) increase in IOP readings that remained above baseline readings for 2 minutes. The results from the steady-state groups and the thiopentone groups support the practice of avoiding succinylcholine with open-globe injuries.

Vinick[8] performed rapid sequence induction with tracheal intubation on 45 patients between the ages of 18 and 65 years old. Three groups of 15 subjects were administered pre-inductions agents and then randomized to receive atracurium 0.5 mg/kg, rocuronium 0.6 mg/kg (a nondepolarizing NMBA), or succinylcholine 1.0 to 1.5 mg/kg for neuromuscular blockade prior to tracheal intubation. Intubation was attempted at 60 seconds after NMBA administration. IOP readings were obtained prior to induction, after the administration of an NMBA, and then again 1-2 minutes after intubation. Between-group comparisons were made using a two-tailed t-test, and a statistical significance was declared at a p-value of less than or equal to 0.05.[8] Compared with the succinylcholine group, the rocuronium group displayed a significant (P=0.046) decrease in IOP from baseline post-induction, prior to intubation. The atracurium group displayed lower IOP values post-induction; however they were not considered significant (P=0.667). An increase in post-intubation values was noted in all groups without exceeding baseline or reaching statistical significance. Rocuronium displayed greater control of IOP pre-intubation, indicating it is a viable alternative to succinylcholine administration in patients requiring intraocular surgeries with general anesthesia.

Smith and Leano[9] compared IOP after induction and tracheal intubation after administration of either pancuronium 0.1 mg/kg (n=8, test group) or d-tubocurarine 3 mg (a nondepolarizing NMBA) before administration of succinylcholine 1.5 mg/kg (n=6, control). In the test group, IOP readings were obtained after the loss of eyelid reflex, 2 minutes after pancuronium administration, and then for 1-minute intervals for 10 minutes. In the control group, IOP readings were obtained after the loss of eyelid reflex, 1 minute after the administration of succinylcholine (3 minutes after the administration of d-tubocurarine), and then again for 1-minute intervals for 10 minutes. The test group displayed a significant (P<0.01) decrease in IOP from induction to 3 minutes post intubation.[9] There was an increase in IOP

from induction to 1 minute post intubation in the control group, however it was not determined to be statistically significant. The results from Smith and Leano[9] conclude that pancuronium lowers IOP compared to succinylcholine that is pre-treated with d-tubocurarine.

A comparison study of 30 patients undergoing surgical procedures, including intraocular procedures, was conducted by Konchigeri et al[10] to determine if pretreatment with pancuronium would attenuate an increase in IOP following succinylcholine administration and tracheal intubation. Prior to induction of anesthesia, the control group (n=15) received saline pretreatment, and the study group (n=15) received pancuronium 1.0 mg. A Schiotz tonometer measured IOP levels at baseline before the administration of succinylcholine 1.0 mg/kg, then 1 minute after the administration of succinylcholine for neuromuscular blockade, and finally, 1 minute after intubation. Student's t-test was applied, and $P<0.05$ was determined to be significant.[10] The control group displayed elevations in IOP above baseline values after succinylcholine administration and intubation, while the test group displayed elevations after intubation only. This study revealed that pretreatment with a nondepolarizing NMBA is useful to attenuate IOP increases post succinylcholine administration. The nondepolarizing agent will not, however, mitigate an increase in IOP following direct laryngoscopy.

Mitra et al[11] performed a randomized, double-blind control study comparing IOP values in 40 patients receiving rapid-sequence intubation without cricoid pressure. This study sought to contrast the effect of rocuronium 0.6 mg/kg (a nondepolarizing NMBA) with that of succinylcholine 1.5 mg/kg administration for neuromuscular blockade with tracheal intubation. IOP levels were obtained with Schiotz tonometry at baseline, after induction, 1 minute after administration of the NMBA, 1 minute after intubation, and then in 1-minute intervals for 3 minutes. Student's t-test with Bonferroni correction was used to compare

IOP values, and $P<0.05$ was considered significant. In the succinylcholine group (n=20), IOP values were significantly elevated above baseline ($P<0.01$) after intubation. IOP values in the rocuronium group (n=20) did not rise above baseline values and remained significantly below baseline values for 5 minutes after induction ($P<0.01$). Mitra et al determined that rocuronium is a good alternative to succinylcholine administration to prevent unwanted elevations in IOP.

A randomized, double-blind study conducted by Chiu et al[12] compared IOP changes with the administration of rocuronium 0.9 mg/kg or succinylcholine 1.5 mg/kg during RSI and tracheal intubation. IOP values were recorded prior to induction, prior to intubation, immediately after intubation, and again for 5 minutes after intubation with a Keeler Pulsair tonometer. Statistical analysis to compare IOP values was performed with a "paired t-test and two-way analysis of variance for repeated measurements…"[12] and a "…probability of less than 0.05 was the criterion for statistical significance."[12] The succinylcholine group (n=15) revealed a significant increase in IOP post induction and intubation ($P=0.01$). The rocuronium group (n=15) displayed a reduction in IOP post induction ($P=0.01$) with an increase in values post intubation; however they did not exceed baseline values. Based on these findings, succinylcholine precipitates an elevation in IOP that is not seen with rocuronium administration.

Discussion

Considering the aforementioned weaknesses of the sole case report and that case reports are weak evidence in general, we focus on discussion of the research studies. Most hierarchies of evidence consider randomized controlled trials and meta-analysis of randomized controlled trials as the strongest evidence. Six studies were compared with a total of 189 subjects undergoing various surgical procedures requiring tracheal intubation that allowed for IOP monitoring. The sample sizes ranged from 14-45 patients, with an age range of 17-70 years.

Nondepolarizing NMBAs were administered to 103 subjects, of whom 50 subjects received rocuronium prior to intubation, 25 subjects received atracurium prior to intubation, 5 subjects received atracurium after intubation, and 23 patients received pancuronium. Succinylcholine was administered to 86 subjects. In 5 of the 6 studies,[8-12] a comparison was made between succinylcholine and a nondepolarizing NMBA. Sedation and induction was achieved by administering either a sedative-hypnotic agent or an opioid agent, or a combination of the two. IOP measurements were obtained at different times among the studies but in general consisted of post-induction (before intubation) and post-intubation time periods.

The nondepolarizing NMBAs displayed a slight consistent superiority to succinylcholine with regards to reducing IOP prior to intubation in three studies,[7-12] Although those particular agents were not able to consistently prevent an increase in IOP *following* intubation, they were able to maintain IOP levels below baseline readings or values obtained with succinylcholine. Rocuronium did attenuate an increase in IOP following intubation in two studies.[11,12] Succinylcholine is not as efficacious as the nondepolarizing NMBAs at preventing elevations in IOP following induction or intubation. Following the administration of succinylcholine and tracheal intubation, IOP readings exceeded baseline readings, and some elevations remained for up to 3 minutes.

The findings of this review offer guidance when considering choice of NMBA for intubation. Although succinylcholine has not been found to definitively cause extrusion of vitreous humor, it remains a theoretical concern as elevations in IOP occur with its administration. Rocuronium is a better choice especially for rapid-sequence induction. The research clearly indicates that rocuronium is the sole paralytic agent that will consistently maintain IOP readings at or below baseline levels after induction and tracheal intubation. Succinylcholine administration provides for efficient intubation conditions but without consistently

maintaining IOP readings at or below baseline readings following induction or intubation.

Atracurium and pancuronium allow IOP maintenance after induction and intubation; however, they may not provide successful intubating conditions, especially for rapid-sequence intubation, making them less desirable for these patients. Rocuronium, at doses of 1-1.5 mg/kg, provides adequate intubating conditions comparable to succinylcholine for rapid-sequence intubation. Tracheal intubation has been found to be the single most important contributing factor to an IOP elevation. Therefore, we should focus on the risk of vitreous humor extrusion during intubation. Fast, efficient, and minimally stimulating intubation is prudent in this patient population. Further research should be conducted to identify any improved intubating modalities (eg, video laryngoscopy, fiberoptic light wand, high narcotic/remifentanyl induction, sympatolytics) and other methodologies that may lessen IOP increases.

Conclusion and Summary

Research and case reports have not been able to create a reliable association between the actual loss of ocular contents and succinylcholine administration. However, succinylcholine has been found to be associated with increased IOP after its administration and after intubation. Nondepolarizing NMBAs, particularly rocuronium, administered prior to, or in place of, succinylcholine have been found to lessen IOP elevation after induction and intubation. Therefore, the research question "in adult patients with open-globe ocular injuries, does the administration of succinylcholine for intubation compared to nondepolarizing NMBAs cause increases in IOP and support the theoretical risk of extrusion of aqueous humor," has been answered affirmatively with the available evidence and considering the following caveats:

- Succinylcholine administration will raise IOP above baseline.
- Nondepolarizing NMBAs do not significantly raise IOP.
- Administration of a nondepolarizing NMBA prior to succinylcholine will attenuate the rise in IOP.
- Laryngoscopy itself is related to more significant increases in IOP than either depolarizing or nondepolarizing NMBAs.
- Clinical considerations and future research should focus on attenuating rises in IOP caused by laryngoscopy.

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